BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Andrew J Griffith	Scientific Director Chief, Otolaryngology Branch Chief, Molecular Biology and Genetics Section
eRA COMMONS USER NAME GRIFFITA	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of California, Davis	BS	1984	Chemistry
Yale University School of Medicine	MD	1992	
Yale University	Ph.D.	1992	Molecular Biophysics and Biochemistry

A. Personal statement

My research program has focused on molecular mechanisms of genetic deafness for over 16 years. We study human families and patients with hereditary disorders of hearing and balance. We map, identify, and characterize the function of the underlying genes. We generate new mouse models or study existing mouse models to understand the pathogenesis of loss of hearing and balance of these disorders with the goal of conceiving, testing and developing potential interventions for these disorders in human patients. As Scientific Director of the National Institute on Deafness and Other Communication Disorders (NIDCD), I serve as Director of the NIDCD Division of Intramural Research. Our Intramural Program has active programs and opportunities for basic and clinical research training and experiences at all levels: high school, college, post-baccalaureate, pre-doctoral medical and graduate students, resident physicians and post-doctoral fellows.

B. Positions and Honors

Positions and Employment

1992-1993	Intern, General Surgery
1993-1998	Resident Physician, Otolaryngology-Head and Neck Surgery, University of Michigan Hospitals
1994-1995	Research Fellow, Human Genetics, University of Michigan School of Medicine
1998-2000	Senior Staff Fellow, Laboratory of Molecular Genetics and Neuro-Otology Branch, NIDCD, NIH
1998-present	Senior Medical Staff, NIH Clinical Center
2000-2006	Tenure-Track Investigator, NIDCD, NIH
2001-2009	Adjunct Associate Professor, Neuroscience and Cognitive Science Program, University of Maryland, College Park
2006-present	Senior (Tenured) Investigator, NIDCD, NIH
2006-present	Chief, Otolaryngology Branch, NIDCD, NIH
2009-present	Scientific Director, NIDCD, NIH
2009-present	Adjunct Professor, Neuroscience and Cognitive Science Program, University of Maryland, College Park
2013-present	Adjunct Professor, Otolaryngology-Head and Neck Surgery, Johns Hopkins School of Medicine
2016-present	Deputy Director for Intramural Clinical Research, NIH
2018-present	Acting Deputy Director, NIDCD, NIH

Honors

1981	CRC Press Freshman Chemistry Achievement Award
1983	National Honor Society of Phi Kappa Phi
1983	Phi Kappa Phi Graduate Fellowship
1983	Clorox Chemical Company Scholarship
1984	Chemistry Departmental Citation for Outstanding Achievement
1990	American College of Rheumatology Medical Student Travel Award

1990	American College of Rheumatology Medical Student Achievement Award
1992	M.D./Ph.D. Prize for Outstanding Graduate of the Medical Scientist Training Program (Yale University)
1996	Association for Research in Otolaryngology Resident Travel Award
1997	Merle Lawrence Research Award for Best Basic Science Research Paper (University of Michigan Otolaryngology Residency program)
1998	Association for Research in Otolaryngology Resident Travel Award
1998	John L. Kemink Award for Best Clinical Research Paper (University of Michigan Otolaryngology Residency program)
2002	Presidential Early Career Award for Scientists and Engineers (PECASE)
2017	NIH Director's Award

Other Experience and Professional Memberships

1985-1992	Editor, *Yale Journal of Biology and Medicine*
1995-present	Member, Association for Research in Otolaryngology
1998-present	Member, American Society of Human Genetics
2000-2003	Physician Research Training Committee, Association for Research in Otolaryngology
2002-2005	Advisory Board, "Summer Program in Genetics for Audiology Faculty" funded by NIH grant 1 R25 05543-01
2005-2011	Scientific Review Committee, The National Organization for Hearing Research Foundation
2005-2010	Associate Editor, *Journal of Medical Genetics*
2009-2011	Board of Visitors, College of Computer, Mathematical, and Natural Sciences (formerly College of Chemical and Life Sciences prior to 2010 merge), University of Maryland
2010-present	Editorial Board, *Journal of Medical Genetics*
2011-2015	Associate Editor, *Journal of the Association for Research in Otolaryngology (JARO)*
2011-present	Editorial Board, *Otology & Neurotology*
2014-present	Member, American Neurotology Society
2015-present	Member, American Otological Society

C. Contribution to Science

1. Identification and characterization of transmembrane channel-like (TMC) genes and proteins. We and our collaborators have identified mutations in human *TMC1* and mouse *Tmc1* as the cause of dominant and recessive hearing loss in humans (DFNA36 and DFNB7/B11) and mice (Beethoven, deafness), respectively. We have shown that *Tmc1* and the closely related *Tmc2* gene encode transmembrane proteins that are essential components of the mechanoelectrical transduction complex at the tips of mammalian hair cell stereocilia.
    a. Kurima, K., L.M. Peters, Y. Yang, S. Riazuddin, Z.M. Ahmed, S. Naz, D. Arnaud, S. Drury, J. Mo, T. Makishima, M. Ghosh, P.S.N. Menon, D. Deshmukh, C. Oddoux, H. Ostrer, S. Khan, S. Riazuddin, L.L. Hampton, P.L. Deininger, J.F. Battey, Jr., B.J.B. Keats, E.R. Wilcox, T.B. Friedman, and A.J. Griffith. 2002. Dominant and recessive deafness caused by mutations of a novel gene, *TMC1*, required for cochlear hair-cell function. *Nat. Genet. 30:277-284*.
    b. Vreugde, S., A. Erven, C.J. Kros, W. Marcotti, H. Fuchs, K. Kurima, E.R. Wilcox, T.B. Friedman, A.J. Griffith, R. Balling, M.H. de Angelis, K.B. Avraham, and K.P. Steel. 2002. Beethoven, a mouse model for human non-syndromic hearing impairment DFNA36/B7/B11. *Nat. Genet. 30:257-258.*
    c. Kawashima, Y., G.S.G. Géléoc, K. Kurima, V. Labay, A. Lelli, Y. Asai, T. Makishima, D.K. Wu, C.C. Della Santina, J.R. Holt and A.J. Griffith. 2011. Mechanotransduction in mouse inner ear hair cells requires transmembrane channel-like genes. *J. Clin. Invest. 121:4796-4809*.
    d. Pan, B., G.S. Géléoc, Y. Asai, G.C. Horwitz, K. Kurima, K. Ishikawa, Y. Kawashima, A.J. Griffith* and J.R. Holt*. 2013. TMC1 and TMC2 are components of the mechanotransduction channel in hair cells of the mammalian inner ear. *Neuron 79:504-515*. (*corresponding authors)
    e. Kurima, K., S. Ebrahim, B. Pan, B.A. Millis, H. Nakanishi, T. Fujikawa, Y. Kawashima, B.Y. Choi, K. Monahan, R. Cui, J.R. Holt, A.J. Griffith* and B. Kachar*. 2015. Transmembrane channel-like 1 and 2 localize at the site of mechanotransduction in mammalian inner ear hair cell stereocilia. *Cell Rep.*

12:1606-1617. (*corresponding authors)

2. Human *SLC26A4* genotypes and phenotypes associated with hearing loss and enlargement of the vestibular aqueduct (EVA). We have ascertained approximately 140 patients and families with EVA at the NIH Clinical Center. Our comprehensive phenotype analyses and *SLC26A4* mutation analyses have revealed strong correlations of the number of mutant alleles of *SLC26A4* with the auditory phenotype, thyroid phenotype, and familial recurrence probability. We have published a series of studies on the genetic epidemiology of hearing loss associated with EVA and *SLC26A4* mutations in a variety of global populations and showed that *SLC26A4* mutations are the second most common known genetic cause of deafness worldwide. We have identified an upstream SLC26A4-linked haplotype that defines the most common deafness-associated allele of any gene in European-Caucasian populations.
    a. Griffith, A.J., H.A. Arts, C. Downs, J.W. Innis, N.T. Shepard, S. Sheldon, S. Gebarski. 1996. Familial large vestibular aqueduct syndrome. *Laryngoscope 106: 960-965.*
    b. Park, H.-J., S. Shautak, X.-Z. Liu, S. Hahn, S. Naz, M. Ghosh, S. Riazuddin, H.-N. Kim, S.-K. Moon, S. Abe, K. Tukamoto, R. Erdenetungalag, J. Radnaabazar, A. Pandya, W.E. Nance, S. Usami, E.R. Wilcox, S. Riazuddin, and A.J. Griffith. 2003. Origins and frequencies of *SLC26A4* (*PDS*) mutations in East and South Asians: global implications for the epidemiology of deafness. *J. Med. Genet. 40:242-248*.
    c. Pryor, S.P., A.C. Madeo, J.C. Reynolds, N.J. Sarlis, K.S. Arnos, W.E. Nance, Y. Yang, C.K. Zalewski, C.C. Brewer, J.A. Butman, and A.J. Griffith. 2005. *SLC26A4* genotype-phenotype correlation: nonsyndromic hearing loss with enlargement of the vestibular aqueduct (EVA) is clinically and genetically distinct from Pendred syndrome. *J. Med. Genet. 42:159-165*.
    d. Choi, B.Y., A.K. Stewart, A.C. Madeo, S.P. Pryor, S. Lenhard, R. Kittles, D. Eisenman, H.J. Kim, J. Niparko, J. Thomsen, K.S. Arnos, W.E. Nance, K.A. King, C.K. Zalewski, C.C. Brewer, T. Shawker, J.C. Reynolds, J.A. Butman, L.P. Karniski, S.L. Alper, and A.J. Griffith. 2009. Hypo-functional *SLC26A4* variants associated with nonsyndromic hearing loss and enlargement of the vestibular aqueduct: genotype-phenotype correlation or coincidental polymorphisms? *Hum. Mutat. 30:599-608.*
    e. Chattaraj, P., T. Munjal, K. Honda, N. Rendtorff, J.S. Ratay, D.S. Risso, I. Roux, E.M. Gertz, A.A. Schäffer, T.B. Friedman, R.J. Morell, L. Tranebjærg, and A.J. Griffith. 2017. A common *SLC26A4*-linked haplotype underlying nonsyndromic hearing loss with enlargement of the vestibular aqueduct. *J. Med Genet. 54:665-673*.

3. Animal models of normal and abnormal endolymphatic sac function and structure (enlargement of the vestibular aqueduct: EVA). We engineered a binary transgenic mouse model of human EVA that recapitulates the asymmetry, delayed onset, and fluctuations that are commonly observed in human pediatric patients with EVA. We and our collaborators have shown that expression of SLC26A4 is required during a critical time window during development, and only in the endolymphatic sac, for the acquisition of normal hearing thresholds at 1 month of age. Although the initial loss of SLC26A4 initially affects the function of the sac, this results in an alteration of the endolymph that secondarily disrupts stria vascularis structure and function, which is the direct cause of fluctuations and loss of hearing. We have defined the single-cell transcriptional architecture and taxonomy of the endolymphatic sac epithelium and a cell type and molecular pathway disrupted by genetic mutations that cause EVA.
    a. Choi, B.Y., H.-M. Kim, T. Ito, K.-Y. Lee, X. Li, K. Monahan, Y. Wen, E. Wilson, K. Kurima, T.L. Saunders, R.S. Petralia, P. Wangemann, T.B. Friedman and A.J. Griffith. 2011. Mouse model of enlarged vestibular aqueducts defines temporal requirement of *Slc26a4* expression for hearing acquisition. *J. Clin. Invest. 121:4516-4525*.
    b. Li, X., J.D. Sanneman, D.G. Harbridge, F. Zhou, T. Ito, R. Nelson, R. Chambrey, D. Eladari, T. Miesner, A.J. Griffith, D.C. Marcus and P. Wangemann. 2013. SLC26A4 targeted to the endolymphatic sac rescues hearing and balance in *Slc26a4* mutant mice. *PLoS Genet. 9:e1003641*.
    c. Ito, T., X. Li, K. Kurima, B.Y. Choi, P. Wangemann and A.J. Griffith. 2014. *Slc26a4*-insufficiency causes fluctuating sensorineural hearing loss and stria vascularis dysfunction. *Neurobiol. Dis. 66:53-65*.

d. Nishio, A., T. Ito, H. Cheng, T.S. Fitzgerald, P. Wangemann and A.J. Griffith. 2016. *Slc26a4* Expression prevents fluctuation of hearing in a mouse model of large vestibular aqueduct syndrome. *Neuroscience: 329:74-82.*
e. Honda, K., S.H. Kim, M.C. Kelly, J.C. Burns, L. Constance, X. Li, F. Zhou, M. Hoa, M.W. Kelley, P. Wangemann, R.J. Morell, and **A.J. Griffith**. 2017. Molecular architecture underlying fluid absorption by the developing inner ear. *eLife 6:e26851*.

4. Genetic modifiers of hereditary hearing loss in humans and mice. I contributed to the first reported mapping of a Mendelian genetic modifier of human hereditary hearing loss, the first identification of a Mendelian genetic modifier of any human disease or disorder, and the mapping of genetic modifiers of cochlear hair cell degeneration in a mouse model of human DFNA36 hearing loss.
   a. Riazuddin, S., C.M. Castelein, Z.M. Ahmed, A.K. Lalwani, M.A. Mastroianni, S. Naz, T.N. Smith, N.A. Liburd, T.B. Friedman, A.J. Griffith, S. Riazuddin, and E.R. Wilcox. 2000. Dominant modifier *DFNM1* suppresses recessive deafness *DFNB26*. *Nat. Genet. 26:431-434.*
   b. Schultz, J.M., Y. Yang, A.J. Caride, A.G. Filoteo, A.R. Penheiter, A. Lagziel, R.J. Morell, S.A. Mohiddin, L. Fananapazir, A.C. Madeo, J.T. Penniston, and A.J. Griffith. 2005. Modification of human hearing loss by plasma membrane calcium pump PMCA2. *N. Engl. J. Med. 352:39-46*.
   c. Noguchi, Y., K. Kurima, T. Makishima, M. Hrabe de Angelis, H. Fuchs, G. Frolenkov, K. Kitamura, and A.J. Griffith. 2006. Multiple quantitative trait loci modify cochlear hair cell degeneration in the Beethoven (*Tmc1*^{Bth}) mouse model of progressive hearing loss DFNA36. *Genetics 173:2111-2119.*

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/andrew.griffith.1/bibliography/48004280/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

2000-present NIDCD Intramural Research Fund NIH Z01DC000060: “Molecular Analysis of Human Hereditary Deafness”

Completed Research Support

1983 University of California President's Undergraduate Fellowship
1985 Yale Medical School Summer Research Award
1985-1992 Yale University Medical Scientist Training Program (NIH 2T32GM007205)
1994-1995 NIDCD National Research Service Award (NIH 5T32DC000024)
1995 Deafness Research Foundation Grant
1996-1998 University of Michigan General Clinical Research Center Pilot Study Grants (NIH M01RR000042)
1999 NIDCD Intramural Research Fund NIH Z01 DC000054: “Analyses of Type XI Collagen in Craniofacial Development and the Auditory System”
1999 NIDCD Intramural Research Fund NIH Z01 DC000055: “Molecular Genetic Analysis of the Mouse Twirler Mutation”
2000-2007 NIDCD Intramural Research Fund NIH Z01 DC000064: “Clinical Analysis of Disorders of Hearing and Balance”